Remarks

Amendments to the Claims

Applicants have added claim 26 which is directed to enhancing the herbicidal activity of a PSII inhibitor at temperatures equal to or above about 25° C. Support for this claim may be found in Table 8 of the Application (p.14). Phytotoxicity of a PSII inhibitor at 3, 5, 7, and 10 days was substantially increased at 25° C and at 35° C by adding sodium salicylate to a PSII inhibitor (atrazine).

Rejection of Claims 20-25 under §103(a) as unpatentable over Klepper and Ryals

The Office Action rejected claims 20-25 under 35 U.S.C. §103(a) as obvious over combined teachings of Klepper and Ryals *et al.* Applicants respectfully traverse the rejection.

The Office Action states that Klepper teaches the combination of salicylate (SA) with PSII inhibiting herbicides in aqueous solution with the test concentration of the PSII herbicide at 300 ppm or 0.03%. According to the Office Action, one of the stated goals was to determine whether SA could act as a synergist. The Office Action states that Klepper concludes that while SA does act as a synergist, other salicylates may be more persistent and, therefore, more practical or effective. Office Action, p. 2. The Office Action admits that Klepper does not explicitly teach application of these combinations to plants as a method of enhancing herbicidal activity. However, the Office Action maintains that Klepper

> clearly suggest(s) the herbicidal method in the paragraph bridging pages 173-174, wherein the accumulation of NO_x is discussed as the mechanism of action for the PI (i.e., PSII) herbicides: "NO_x evolution is closely related to intact leaf nitrite content. Free nitrite, nitrous acid, and free radical NO_x gases are highly toxic to

> basic plant metabolic systems." (footnotes omitted). Thus, while not testing the combinations on intact, live plants, Klepper clearly suggests that the application of SA will synergistically enhance the activity of PSII herbicides.

The Office Action characterizes Ryals *et al* as teaching that SA, acibenzolar (BTH), and other compounds are known activators of systemic acquired resistance (SAR). The Office Action states that one would be motivated to substitute the SA of Klepper with a compound such as acibenzolar because Ryals *et al* teach their equivalent activity in plants as SAR activators. According to the Office Action, it would have been obvious to have combined SA or other SAR inducers with PSII inhibiting herbicides because Klepper suggests the enhanced herbicidal utility of such compositions and because SA and acibenzolar are both known signaling molecules which are useful for stimulating SAR in plants.

Applicants respectfully disagree. A person skilled in the art would not have been motivated to combine Klepper and Ryals *et al* teaching to arrive at a method of enhancing the herbicidal activity of PSII inhibitors by adding a salicylate because, contrary to the Office Action's suggestion, the accumulation of NO_x is not the mechanism of action of PSII inhibitors. While Klepper does say that NO_x gases are highly toxic to basic plant metabolic systems, nowhere does Klepper say or suggest that PSII inhibitors act through the accumulation of NO_x. To the contrary, Applicants' experiments, as detailed in the Declaration by Paul Silverman, an inventor of the present Application, submitted herewith under 37 C.F.R. §1.132, clearly demonstrate that PSII inhibitors act through a different mechanism, and moreover, NO_x may have a detrimental effect on the activity of PSII inhibitors.

As the Declaration explains, Klepper's own data demonstrate that NO_x does not accumulate when plants treated with PSII inhibitors are incubated in light. (See Klepper, Table I, p. 177). However, PSII inhibitors act only in a light environment. Applicants' data demonstrate that light is needed for atrazine (a typical PSII inhibitor) activity. (See Table 7 in the present Application). Therefore, because PSII inhibitors are effective in a light environment and NO_x does not accumulate when plants treated with PSII inhibitors are incubated in light, it necessarily follows that PSII inhibitors act through a mechanism unrelated to NO_x.

Moreover, Applicants ran the experiment to demonstrate that NO_x decreases, rather than increases, salicylate potentiation of atrazine on tobacco plants. (See Declaration, p.2). As the Declaration discusses, this is consistent with salicylate/NO interaction in animal systems, where salicylates have been reported to be efficient scavengers of NO in mammalian cells and inhibitors of the transcription of NOS2.

Also, Klepper's own statement suggests that while salicylic acid (and therefore, salicylate) "has the ability to act as synergist," (for NO_x production) it cannot be used successfully in field experiments.

> While salicylic acid has the ability to act as a synergist, this study does not necessarily suggest that salicylic acid can be used successfully in field experiments. Free salicylic acid appears to be short lived in leaf tissue.(footnotes omitted). (Klepper, p. 178).

However, Applicants' data demonstrate that to the contrary, sodium salicylate is an excellent atrazine synergist for herbicidal activities (not through NO_x), and therefore, can be used successfully in field experiments.

In summary, PSII potentiation by salicylate is not suggested by Klepper. NO_x accumulation is not induced in light by either PSII inhibitors or sodium salicylate. The inhibition of salicylate potentiation of atrazine by NO indicates a separate and distinct mechanism for salicylate activation of herbicidal activity.

Similarly, the Office Action relies on Ryals *et al* to argue that since SA and other compounds are known activators of SAR, a person skilled in the art would have been motivated to substitute the SA of Klepper with a compound such as acibenzolar. However, as Applicants demonstrated through experiments detailed in the Declaration, SA and other compounds potentiate PSII inhibitors through a pathway which is different than SAR pathway.

To demonstrate that potentiation is occurring through SAR pathway, Applicants used *npr1* plant mutants which lack the ability to induce PR proteins which are necessary for SAR. (See Declaration, p. 4-5). If potentiation were through SAR pathway, then potentiation would not have been observed in the mutants (because they lack the ability to produce SAR). In contrast, Applicants observed that treatment of the mutants with salicylate and atrazine resulted in atrazine potentiation which was very similar to the potentiation in SAR-capable plants. *Id.* Therefore, Applicants conclusively demonstrated that potentiation is occurring through a pathway which is independent from and unrelated to SAR pathway.

Therefore, a person skilled in the art would not have been motivated to use compounds which are known to activate one pathway (SAR) as substitutes for the compounds which participate in another pathway (potentiation of PSII inhibitors). Applicants' claims are drafted to a "method of enhancing the herbicidal activity" of PSII inhibitors. A reference which is completely silent about the method of enhancing the herbicidal activity may not render the method claim obvious. Applicants stress that they are not claiming the combinations *per se*, rather the claims are to novel methods of using the combinations.

Favorable consideration and allowance of claims 20-26 is respectfully requested.

Respectfully submitted,

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